UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
LUFKIN DIVISION

IOVATE HEALTH SCIENCES, INC., UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC. and FLAMMA SpA, Plaintiffs, v. BIO-ENGINEERED SUPPLEMENTS & NUTRITION, INC., d/b/a BSN, INC., and MEDICAL RESEARCH INSTITUTE, Defendants.	Civil Action No. 9:07-CV-46 JUDGE RON CLARK

BSN'S MOTION FOR SUMMARY JUDGMENT THAT THE ASSERTED CLAIMS OF THE '199 AND '287 PATENTS ARE INVALID

Executive Summary

The two patents-in-suit, U.S. Patent No. 5,973,199 (the ô199 patent) and U.S. Patent No. 6,100,287 (the ô287 patent) relate to dietary supplements. The ô199 patent claims hydrosoluble salts of creatine formed from four specific acid anions: citrate, maleate, fumarate or malate. The ô287 patent discloses and claims the use of supplements containing an amino acid and a ketoacid to enhance athletic muscle performance or recovery from fatigue. Because the invention of the ô199 patent was clearly obvious in view of the prior art and the invention of the ô287 patent had been published and publicly used prior the patentôs priority date, the patents in suit are invalid. Defendant Bio-Engineered Supplements & Nutrition, Inc. (ñBSNò) requests that the Court grant summary judgment in this cause as to Plaintiffsô claims of patent infringement due to the invalidity of the ô199 and ô287 patents.

Issues Presented

Whether the patents in suit are invalid under 35 U.S.C. §§ 102 and 103 because

a) The invention of the ô199 patent would have been obvious to a person of ordinary skill in the art. 35 U.S.C. § 103.

b) The invention of the ô287 patent was known, published, and publicly used prior to the patentôs priority date. 35 U.S.C. § 102(a), (b).

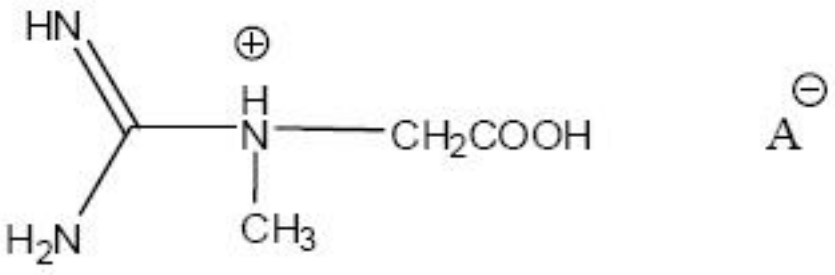
c) To the extent any invention of the ô287 patent is not anticipated under 35 U.S.C. § 102, such invention would have been obvious to a person of ordinary skill in the art. 35 U.S.C. § 103.

Statement of Undisputed Material Facts

A) The ’199 Patent – Claim 1

1. The inventors of the ô199 patent sought to solve the problem of low solubility of creatine. (Exh. A, col. 1, ll. 33-45).[1]

2. Claim 1 of the ô199 patent claims hydrosoluble salts of the formula



3. Wherein A- represents the anion of citric, maleic, fumaric or malic acid. (Exh. A, col. 2, ll. 41-48).

4. The international parent application, through which the ô199 patent claims an earlier filing date, also claimed tartaric acid as one of the anions for the creatine salt. (Exh. B at 4, claim 5).

B) The ’199 Patent – The Berge Reference

1. Creatine supplements became popular in the 1990ôs among people looking to build muscle mass and/or improve athletic performance. (Hamilton Decl., ¶10).

2. Historically (and as of August 4, 1994, the date the foreign parent application of the ô199 patent was filed in Italy), the creatine commonly used in such supplements was in the form of creatine monohydrate. Creatine monohydrate does not dissolve well in water. (*Id.*).

[1] References herein to the lettered Exhibits A-X are to the Exhibits to the Declaration of William J. Hallihan, filed concurrently herewith as Exhibit 1.

3. The goal of the inventors of the ô199 patent as originally stated in the patentôs international parent application was to solve the problem of low solubility of creatine in order to make creatine more available to a human subject. (Exh. B at 1-2; see also Exh. A, col. 1, ll. 33ï 45).
4. The article ñPharmaceutical Saltsò by Stephen M. Berge et al. (ñBerge Referenceò) was published in the Journal of Pharmaceutical Sciences, Vol. 66, No. 1, January 1977. (Hallihan Decl., ¶ 9; Exh. H).
5. The Berge Reference was not before the Examiner during the prosecution of the ô199 patent. (Exh. A at 1, ñReferences Citedò/ñOther Publicationsò).
6. The Berge Reference teaches that salts made with dicarboxylic acids confer greater water solubility than other salts, while salt combinations with monocarboxylic acids are insoluble in water. (Exh. H at 2, ¶ 4).
7. The creatine salts claimed in the ô199 patent are all made with dicarboxylic acids, with the exception of creatine citrate which is a tricarboxylic acid. (Buynak Decl., ¶¶ 15-16; Exh. N at 91, ll. 7-18).
8. One of ordinary skill in the art would have known at the time of the ô199 patentôs invention that maleic, malic, and fumaric acids were dicarboxylic acids and that citric acid was a tricarboxylic acid. (Buynak Decl., ¶¶ 19-21).
9. The Berge Reference presents a table (ñTable Iò) of commercially marketed salts approved for use by the United States Food and Drug Administration, listing such salts and their share of the commercial marketplace through 1974. (Exh. H at 2).

10. Citrate, fumarate, malate, maleate, and tartrate are included in Table I of the Berge Reference. Table I shows that citrate, maleate and tartrate were in widespread use in the commercial market place. (Exh. H at 2).

C) The '199 Patent – The Almada Reference

1. U.S. Patent No. 5,627,172 to Almada et al. is directed to the use of creatine derivatives for reducing cholesterol. Useful creatine derivatives are said to include creatine monohydrate as well as ñpharmaceutically acceptable creatine salts or complexes such as creatine hydrochloride or creatine complexes with other acids.ò (Exh. I at 1, abstract, col. 3, ll. 52-55).
2. A preferred embodiment of the Almada Reference calls for the creatine derivative to be prepared in powdered form and dissolved in a liquid beverage. Almada notes that in cold liquid the powdered creatine derivative typically will not completely dissolve. (Exh. I, col. 4, ll. 41-55).
3. During the prosecution history of the ô199 patent, the Examiner rejected claim 1 as invalid as obvious over Almada in view of Wittman. In response, the inventors submitted evidence of an experiment performed by one of the coinventors (ñthe Del Corona Studyò) which allegedly showed that the inventorsô creatine citrate salt when dissolved in water degraded into the substance creatinine less rapidly and to a lesser extent than creatine hydrochloride, a salt named in the Almada reference. The co-inventor who performed the experiment contended the difference was ñstriking, unexpected, [and] beneficial.ò Based upon this evidence, the Examiner removed the Almada rejection and allowed the patent to issue. (Exh. C at 2-3; Exh. E at 2-3; Exh. F at 2-4; Exh. G).

4. In the Del Corona Study, at the time immediately after the dissolution of the salts in water, 99.66% of the creatine was reported as still remaining in the creatine hydrochloride solution compared to 99.91% for the creatine citrate. An hour after the preparation of the solutions, 99.55% of the creatine was reported as still remaining in the creatine hydrochloride compared to 99.84% for the creatine citrate. (Exh. F at 3).

D) The '199 Patent -- the 1920's Literature

1. The article ñCXV. The Creatine-Creatinine Equilibrium. The Apparent Dissociation Constants of Creatine and Creatinineò by Robert Keith Cannan and Agnes Shore (ñCannan and Shoreò) was published in Biochemical Journal, Vol. 22, pp. 920-929 (1928) (Hallihan Decl., ¶ 12; Exh. K).
2. The article ñThe Equilibrium Between Creatine and Creatinine, In Aqueous Solution. The Effect of Hydrogen Ionò by Graham Edgar and H.E. Shiver (ñEdgar and Shiverò), was published in the Journal of the American Chemical Society, Vol. 47, pp. 1179-1188 (1925). (Hallihan Decl., ¶ 13; Exh. L).
3. The article ñThe Kinetics of the Conversion of Creatine Into Creatinine In Hydrochloric Acid Solutionsò by Graham Edgar and R.A. Wakefield (ñEdgar and Wakefieldò) was published in the Journal of the American Chemical Society, Vol. 45, pp. 2242-2245 (1923). (Hallihan Decl., ¶ 14; Exh. M).
4. None of the three articles identified above in this section were before the Examiner during the prosecution of the ô199 patent. (Exh. A at 1, ñReferences Citedò/ñOther Publicationsò).
5. Cannan and Shore reported a series of experiments comparing creatine degradation at different pH levels over time, all performed at 30 degrees Celsius. At the 25 hour point, degradation to creatinine ranged from approximately 1% to a maximum of

approximately 7% (the maximum occurring at circa 3.0 pH). (Buynak Decl., ¶ 28-29; Exh. K at 924-26).

E) The ’287 Patent

1. The õ287 patent claims the method of administering a composition comprised of amino acids and ketoacids (of differing specificity) to enhance muscle performance or recovery from fatigue. (Exh. P, col. 16, l. 60 ï col. 18, l. 20).
2. Flex Magazine is a periodical directed to bodybuilders and other athletes. The magazine is published on a monthly basis, and features advertisements for nutritional dietary supplements for use in enhancing muscle performance and/or improving recovery from fatigue. (Earnest Decl., ¶ 15, Exh. Q through U).
3. The June 1995 issue of Flex Magazine includes an advertisement for a nutritional supplement named ñTwinLab Mass Fuelò which teaches use of the supplement for improving muscle performance and recovery from fatigue. The supplement is said to contain the ingredients L-Ornithine Alpha-ketoglutarate, Ketoisocaproate acid, L-Glutamine, and L-Carnitine. (Earnest Decl., ¶ 16; Exh. Q at 107).
4. The June 1996 issue of Flex Magazine includes an advertisement for a nutritional supplement named ñWeider Professional Proteinò which teaches use of the supplement for improving muscle performance and recovery from fatigue. The supplement is said to contain the ingredients Arginine Asparate, Ornithine Alpha-ketoglutarate, Alpha-Ketoisocaproic Acid (KIC), Glutamine, and Carnosine. (Earnest Decl., ¶ 26; Exh. R at 138-140).
5. The January 1995 issue of Flex Magazine includes an advertisement for a nutritional supplement named ñNational Health Products Hot Stuff Double Xò which teaches use of the supplement for improving muscle performance and recovery from fatigue. The

supplement is said to contain the ingredients OKG, arginine pyroglutamate, and creatine. (Earnest Decl., ¶ 34; Exh. S at 213-214)

6. The February 1994 issue of Flex Magazine includes an advertisement for a nutritional supplement named ñTwinLab Anti-Catabolic Fuelò (as well as other supplements) and teaches use of the supplement for improving muscle performance and recovery from fatigue. The supplement is in capsule form and said to contain the ingredients L-Ornithine Alpha-ketoglutarate, Ketoisocaproate and L-Glutamine. (Earnest Decl., ¶ 39; Exh. T).
7. The November 1993 issue of Flex Magazine includes two advertisements for a nutritional supplement named ñWeider Performance OKGò which teaches use of the supplement for improving muscle performance and recovery from fatigue. The supplement is in capsule form and said to contain the ingredients L-Ornithine Alpha-ketoglutarate. (Earnest Decl., ¶ 44; Exh. U at 84-85, 176).
8. The book ñThe Anabolic Dietò was written by Dr. Mauro Di Pasquale and published in 1995. In ñThe Anabolic Dietò the author recommends a number of ñformulasò to be taken by an athlete before, during, or after workouts for the purpose of improving muscle performance and recovery from fatigue. ñFormula 1ò is recommended to be prepared in water and is said to include the ingredients OKG (ornithine alpha-ketoglutarate), KIC (ketoisocaproate), glutamine and leucine. ñFormula 3ò is said to contain the ingredients KIC, OKG, arginine and glutamine (as well as other ingredients). (Earnest Decl., ¶¶ 50-51 and 53-56; Exh. V at 56-59).
9. Arginine and Ornithine are each amino acids which can be cationic or dibasic. (Earnest Decl., ¶ 11).

10. Alpha-ketoglutarate is a ketoacid. (Earnest Decl., ¶ 12).

11. Ornithine Alpha-ketoglutarate is an amino acid conjugated with a ketoacid. (Earnest Decl., ¶ 13).

12. Glutamine is an amino acid. (Earnest Decl., ¶ 11).

13. Ketoisocaproic Acid (KIC)/ketoisocaproate is a ketoacid. (Earnest Decl., ¶ 12).

14. Strength is a measure of muscle performance. (Earnest Decl., ¶¶ 14, 35, 55; Exh. P, col. 16, ll. 1-4).

15. Increasing muscle mass enhances muscle performance. (Earnest Decl., ¶ 22).

16. Preventing breakdown in muscle tissue that would otherwise occur enhances muscle performance and recovery from fatigue. (Earnest Decl., ¶ 51).

17. It was known at the time of the invention by those of ordinary skill in the art that nutritional dietary supplements of the type claimed in the õ287 patent could be prepared in capsule form. (Earnest Decl., ¶ 57).

18. It was known at the time of the invention by those of ordinary skill in the art that nutritional dietary supplements of the type claimed in the õ287 patent could be prepared in low calorie solutions. (Earnest Decl., ¶¶ 43, 49, 56, 58).

Argument

A. Summary Judgment Is Appropriate for the ’199 Patent Because There Is No Genuine Issue of Material Fact Regarding Invalidity Under 35 U.S.C. § 103.

The granting of summary judgment of invalidity is appropriate under 35 U.S.C. § 103. *See Ecolochem, Inc. v. Southern Cal. Edison Co.*, 227 F.3d 1361 (Fed. Cir. 2000). A patent claim is invalid if the subject matter of the claim would have been obvious at the time of the invention in view of the prior art to one of ordinary skill in the art. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). ñThe combination of familiar elements with

known methods is obvious when it provides no functionality except for yielding predictable results.ò *AdvanceMe, Inc. v. RapidPay, LLC*, 509 F.Supp.2d 593, 610 (E.D. Tex. 2007).

1. The Berge Reference, Not Considered During Examination, Clearly Renders Claim 1 of the ’199 Patent Obvious.

The inventors of the ô199 patent sought to increase the solubility of a long-known compound: creatine. The Berge reference is so clear as to how to accomplish this goal that a layman with a good chemical dictionary could have applied it and quickly identified the salts claimed in the ô199 patent.

In a section titled ñPotentially Useful Salts,ò the Berge Reference states:

> ñ**Knowledge that one salt form imparts greater water solubility...would greatly benefit chemists and formulators**....[I]n general**,** salt combinations with monocarboxylic acids are insoluble in water and lend themselves to repository preparations, **while those of dicarboxylic acids confer water solubility if one carboxylic group is left free**.ò

(Exh. H at 2 (emphasis added).

As was discussed during the claim construction briefing and at the March 5, 2008 claim construction hearing, malic acid, maleic acid, and fumaric acid are known to be dicarboxylic acids, while citric acid is a tricarboxylic acid. (Buynak Decl., ¶ 15-16; Exh. N at 91, ll. 7-18).[2] Tartaric acid, which was additionally claimed as an acid anion in the ô199 patentôs parent foreign application, was also a known dicarboxylic acid. (Buynak Decl., ¶. 16).

Leaving nothing to doubt, the Berge reference also provides a table of commercially marketed salts approved by the U.S. Food and Drug Administration. (Exh.

[2] For the claimed salts in their 1:1 molar ratio form (e.g., creatine malate, as compared to dicreatine malate), a carboxylic group is left free. (Buynak Decl., at ¶ 17) It is undisputed that claim 1 does not include creatine salts in 1:1 molar ratio with the respective anions.

H at 2, Table I). Each of the acid salt forms claimed by the ô199 patent are listed. Of the dicarboxylic acids included in the table, maleic acid and tartaric acid were disclosed as being in the most widespread use. (*Id.*; Buynak Decl., ¶ 21). Clearly it would be obvious for one of ordinary skill in the art seeking to increase the solubility of creatine to apply the Berge reference to create the dicarboxylic acid salts of creatine claimed in the ô199 patent. (Buynak Decl., ¶ 25).

Against this unambiguous record of obviousness, Plaintiffs may attempt to invoke the ñteaching awayò argument which was unsuccessfully argued to the Examiner during prosecution in response to the rejection for obviousness based on the Almada reference (discussed *infra* at subsection 2). Specifically, Plaintiffs may argue that prior to their invention, the inert substance creatinine was present in all creatine acid salts (both for salts formed with strong mineral acids, such as creatine hydrochloride, and for salts formed with weaker organic acids such as the ones claimed in the ô199 patent). The inventors alleged during prosecution that the lack of sufficient creatine in these impure salts, as well as the degree of creatine degradation that occurs when the salts are dissolved in water, made any creatine acid salts suggested by the prior art unsuited for the purpose stated in the application, i.e., providing a therapeutic dose of creatine to a human subject at necessary concentrations. (Exh. D at 4-6).[3]

The record refutes such a contention. As this Court is aware, claim 1 has been construed as requiring a level of purity only such that ñthe salt of creatine is present in a concentration chosen by the person preparing the salt.ò (Exh. O at 9). There is no evidence that the ñtraditionalò methods of preparing creatine salts decried by the

[3] The '199 patent states that for the purposes described one would seek to administer doses of 5-10 grams of creatine. (Exh. A, col. 1, ll. 38-39).

inventors during prosecution of the ô199 patent resulted in more than trivial amounts of creatinine in the salts, let alone degraded the creatine to the extent that the salts could not be used to deliver the doses of creatine in question, *especially* in light of the gains in providing creatine to the subject that would be achieved from increasing solubility of the creatine. In fact, the record shows just the opposite. (Buynak Decl., ¶ 27-32). For example, the Cannan and Shore reference discloses that in a 25 hour period, one would expect, at worst, a loss of 7% of the creatine to creatinine when in solution with an acid. (Buynak Decl., 28-29; Exh. K at 924-26).[4]

In actuality, salification of creatine with organic acids occurs well before 25 hours, but this ñworst case scenarioò shows how untenable any teaching away argument based on creatinineôs presence in the salts would be. (Buynak Decl., ¶ 30). Even in the fanciful scenario where one of ordinary skill in the art chose to make a salt with a minimum purity of 50% creatine, the increase in solubility of the creatine (reported by the ô199 patent to be 300 to 1500% at col. 1, ll. 50-53) would more than make up for any reasonably conceivable loss to creatinine. A prior art reference only creates a ñteaching awayò if it suggests a path of development ñis unlikely to be productive of the result sought by the applicant.ò *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006), *citing In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

[4] During prosecution, while the inventors of the ô199 patent argued that one would expect creatinine to be formed when making either a mineral acid salt of creatine or an organic acid salt of creatine, nothing was contended (let alone evidence presented) regarding the level of creatinine ñimpurityò that would be expected, or even which of the two types of creatine acid salts would have been expected to contain more creatinine. (Exh. D at 4-6). The Examiner refused to even consider the argument regarding the alleged greater purity of the claimed salts because the inventors had not claimed creatine salts pure of creatinine. (Exh. E at 2).

2. The Examiner's Rejection Over Almada in View of Wittman Was Proper and Would Not Have Been Removed Had the Berge Reference Been Presented.

There are several reasons why the ô199 patent should have been rejected as obvious over the Almada patent (U.S. Patent No. 5,627,172, Exh. I). First, as the Examiner correctly maintained, the Almada patent explicitly teaches the use of a pharmaceutically acceptable salt of creatine. (Exh. E at 2, *citing* Exh. I (Almada), col. 3, l. 52). Moreover, the specific pharmaceutical acids named in the ô199 patent were specified in the Wittman reference (U.S. Patent No. 5,489,589) (Exh. C at 3, *citing* Exh. J (Wittman), col. 6, ll. 8-24), clearly creating a prima facie case of obviousness. The Examiner only removed the rejection upon the declaration of co-inventor Del Corona, who provided results of an experiment purporting to show that the creatine in one of the claimed salts (creatine citrate) when dissolved in water degraded to creatinine less rapidly and to a lesser extent than did the creatine hydrochloride salt mentioned in Almada. (Exh. F, G).

There are several reasons why rejection based on Almada should have been maintained. *Assuming arguendo* that the results of the Del Corona experiment were indeed unexpected, they were not sufficiently material as a matter of law to overcome the Examinerôs prima facie case of obviousness. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007), *citing Newell Cos., Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 768 (Fed. Cir. 1988) (even if invention exhibits unexpectedly superior results, such a showing cannot overcome strong showing of obviousness); *McNeil-PCC, Inc. v. Perrigo* Co., 516 F.Supp. 2d 238, 255 (S.D.N.Y. 2007), affôd without opinion, 2008 U.S. App. LEXIS 8017 (Fed. Cir. Apr. 14, 2008) (unexpected result of improved stability for

therapeutic compound could not outweigh obviousness of the claimed invention for purpose of masking compoundôs bitter taste).

Almada teaches that in a preferred embodiment, the creatine derivative will be in powdered form, dissolved in a liquid, and prepared at approximately the time of intended use and consumption by a human patient. (Exh. I, col. 4, ll. 41-48). Almada mentions that the creatine derivative would not typically fully dissolve in cold liquids (Exh. I, col. 4, ll. 53-55). Yet in the Del Corona experiment, at the time of consumption (the initial measuring after the two creatine salt solutions had been prepared), the difference in degradation of just such compositions as described in the Almada patent was reported to be a mere quarter of one percent (0.25 %). (Exh. F at 3). After one hour the difference was only 0.29%. (*Id.*). Such minute degradation would not be of significant relevance to one seeking to use a pharmaceutical salt of creatine for the therapeutic purposes in question. (Buynak Decl., ¶ 31; Hamilton Decl., ¶12-13).

Second, the prima facie case for obviousness based on Almada is even stronger than what was considered by the Examiner. In choosing a pharmaceutically acceptable creatine salt as called for by Almada, one of ordinary skill in the art would desire a salt that was available, safe, and soluble. As noted, the Almada reference itself raises the issue of the low-solubility of creatine powders dissolved in water. (Exh. I, col. 4, ll. 53-55). The Berge reference discussed *supra* would have directed one of ordinary skill in the art to the dicarboxylic salts claimed in the ô199 patent, as well as simply providing a list of FDA approved salts which included commonly used salts such as citrates and maleates.[5]

[5] The decision in *Pfizer v. Apotex* is also notable in that the Federal Circuit relied in-part on the same Berge reference at issue here, particularly the table of FDA-approved acid salt forms, to hold a patented

B. The ’287 Patent Is Anticipated or Rendered Obvious By the Use of Amino Acid-Ketoacid Supplements Disclosed in Fitness Periodicals Published Years Before the Earliest Possible Effective Filing Date of the Patent.

The ô287 patent is directed to the use of compounds comprising an amino acid and a ketoacid for the purpose of increasing muscle performance or reducing muscle fatigue. Pursuant to the Courtôs claim construction order dated June 5, 2008, amino acids and ketoacids are construed to include their salt forms.

35 U.S.C. § 102 states:

A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.

The use of the amino acid / ketoacid compounds claimed by the ô287 patent was widespread among bodybuilders long prior to November 13, 1996 (a year prior to the earliest date of application which Plaintiffs are permitted to assert for the ô287 patent).[6] Such use was clearly, even starkly, disclosed in legions of popular fitness publications dating as early as 1993. Many of the amino acids and ketoacids identified in the ô287 patent are explicitly named in advertisements for nutritional supplements used to improve muscle performance or enhance recovery from fatigue. The 1995 book ñThe Anabolic Dietò by Dr. Mauro Di Pasquale also clearly disclosed the use of the amino acid/ketoacid

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pharmaceutical salt obvious as a matter of law. Plaintiff had acquired a patent on the salt amlodipine besylate, which it had formulated after discovering undesirable properties with its previously patented amlodipine salt (i.e., amlodipine maleate). *Pfizer*, 480 F.3d at 1353-54. There, as here, the prior art indicated that the claimed acid form for the salt (besylate) would provide superior characteristics. The Federal Circuit noted that this evidence of obviousness was bolstered by the list of FDA-approved salts in Berge, as it was commonplace for formulators to use such a compendium to produce new drug formulations. *Id.* at 1363. The Court further implied that use of the more frequently marketed salts listed in Berge would be particularly obvious. *Id*. This is precisely what occurred in the present case: three of the salts originally claimed by the inventors of the ô199 patent are among the most widely used as disclosed by Berge. (Exh. H at 2, Table I).

[6] The ô287 patent claims priority to Provisional Application No. 60/065,429, filed November 13, 1997. BSN disputes that any claim of the ô287 patent other than claim 3 is entitled to this date due to lack of support in the provisional application for the broader claims. Regardless, all prior art presented in the present motion was published prior to November 13, 1996).

compounds claimed in the õ287 patent. To the extent some of the minor variations of the invention presented in the dependent claims of the õ287 patent were not explicitly disclosed in these publications, they involve insignificant variations that would have been obvious to those of ordinary skill in the art. Only claim 3 (which requires the specific amino acid glycine to be present in the compound) requires a combination of references to establish invalidity for obviousness under 35 U.S.C. § 103.[7]

The following chart summarizes which elements specifically identified in the õ287 patent appear in the prior art references submitted in this motion.[8]

[7] The parties currently dispute which ñten claimsò are at issue in the current action. Plaintiffs have unilaterally chosen 10 claims on the condition that Defendants drop their declaratory judgment of invalidity counterclaims for the remaining claims. For purposes of this motion, BSN only seeks to invalidate Plaintiffsô asserted claims. *Dkt. No.* 173.

[8] Each of the compounds identified in the charted references are consumed orally (claim 9) and administered to a human subject (claim 18).

Claim # / Element / Reference	1 Ketoacid	1 Cationic or dibasic amino acid	2 Glutamate, glutamine, or glycine	5 Ketoiso-caproate (KIC)	7 Arginine	8 Conjuga-ted amino acid and ketoacid	10 Low calorie beverage	12 Cap-sule
1 (Mass Fuel)	✓ Alpha-ketoglutarate; Ketoisocapr-oate	✓ Ornithine	✓ Glutamine	✓		✓ OKG		
2 (Professio-nal Protein)	✓ Alpha-ketoisocapr-oic acid	✓ Ornithine; Arginine	✓ Glutamine	✓	✓	✓ OKG		
3 (Hot Stuff Double X)	✓ Alpha-ketoglutarate	✓ Ornithine; Arginine pyroglutam-ate			✓	✓ OKG		
4A (Anti-Catabolic Fuel)	✓ Ketoisocap-roate	✓ Ornithine	✓ Glutamine	✓		✓ OKG		✓
4B (Performa-nce OKG)	✓ Alpha-ketoglutarate	✓ Ornithine				✓ OKG		✓
5 (ñThe Anabolic Dietò) Formula 1	✓ Alphta-ketoglutarate; Ketoisocapr-oate	✓ Ornithine; Arginine	✓ Glutamine	✓		✓ OKG	✓	
5 (ñThe Anabolic Dietò) Formula 3	✓ Alpha-ketoglutarate; Ketoisocapr-oate	✓ Ornithine; Arginine	✓ Glutamine	✓	✓	✓ OKG	✓	

1. The June 1995 Advertisement for TwinLab Mass Fuel Anticipates Claims 1, 2, 5, 8, 9, and 18.

The June 1995 issue of Flex Magazine includes an advertisement for a nutritional supplement named ñMass Fuel.ò (Earnest Decl., ¶ 16; Exh. Q at 107). The advertisement stated that Mass Fuel included the following ingredients:

- L-Ornithine Alpha-ketoglutarate
- Ketoisocaproate acid (KIC)
- L-Glutamine
- L-Carnitine

Id. The advertisement states that the supplement had helped top professional athletes ñgain size, strength and a real competitive edge.ò *Id.* The advertisement further teaches that using the supplement promotes ñmuscle synthesis and growth,ò and that research indicated that the supplement prevents muscle breakdown during workouts and speeds muscle recovery afterwards. *Id.*

Claim 1 of the õ287 patent recites:

ñA method for enhancing muscle performance or recovery from fatigue wherein said method comprises administering a composition comprising a ketoacid and an amino acid wherein said amino acid is cationic or dibasic.ò (Exh. P, col. 16, ll. 61-64).

Every element of the method claimed in claim 1 is found in the Mass Fuel advertisement. It is undisputed that ornithine is an amino acid which is ñcationic or dibasicò and that alpha-ketoglutarate and ketoisocaproic acid are ketoacids. Increase in muscle strength is by definition an enhancement in muscle performance, and accelerated muscle recovery is synonymous with recovery from muscle fatigue. (Earnest Decl., ¶¶ 14, 22, 24, 35, 51, 55; Exh. P, col. 16, ll. 1-4).

Anticipation of other claims is just as readily apparent. The only additional limitation in claim 2 of the õ287 patent is that the compound include either glutamate, glutamine or glycine. (Exh. P, col. 16, ll. 61-67). Mass Fuel contains glutamine.

Claim 5 is specifically limited to a-ketoisocaproic acid and thus is also anticipated. (Exh. P, col. 17, ll. 8-9; Earnest Decl., ¶¶ 16, 18, 20-25).

Claim 8 is a dependent claim of claim 1, with the limitation that the amino acid and ketoacid are conjugated. (Ex. P, col. 17, ll. 15-16). The ingredient ornithine alpha-ketoglutarate is just such a conjugate compound. (Earnest Decl., ¶¶ 13, 19). In fact, the similar ingredient arginine alpha-ketoglutarate has been identified by Plaintiffs as

infringing this claim in conjunction with BSN product advertising similar to the advertisements presented in this motion. (Exh. W at 18, discussion of claim 8). A maxim of patent law states that which literally infringes if later in time anticipates if earlier. *Schering Corp. v.Geneva Pharms., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003).

Claim 9 is a dependent claim of claim 1, with the limitation that the compound is administered orally. (Exh. P, col. 17, ll. 17-18). Mass Fuel is administered orally, as indicated in the advertisement that it may be mixed with water. (Earnest Decl., ¶ 20).

Claim 18 is a dependent claim of claim 1, with the limitation that the method is to be used on a human. (Exh. P, col. 18, ll. 16-17). Though probably self-evident, the advertisement features testimonials from actual human users. (Earnest Decl., ¶ 20).

Accordingly, this reference anticipates claims 1, 2, 5 and 8 of the ô287 patent. (Earnest Decl., ¶¶ 16-25).

2. The June 1996 Advertisement in Flex Magazine for Weider Professional Protein Anticipates Claims 1, 2, 5, 7, 8, 9, and 18.

Weider Professional Protein is a supplement similar to Mass Fuel, with the important distinction that it includes the amino acid arginine as well as ornithine, thus additionally anticipating claim 7. An advertisement for Professional Protein in the June 1996 issue of Flex Magazine states that the product contains the following ingredients:

- Arginine Asparate
- Ornithine Alpha-Ketoglutarate
- Alpha-Ketoisocaproic (KIC) Acid
- Carnosine
- Glutamine (identified as an ingredient on p. 140, ¶ 4)

(Exh. R at 139-140).

The advertisement provides testimonials from users that the supplement ñhelps me recuperate faster from my workoutsò (Lou Ferrigno), ñmy recuperation is better, and I feel better after severe workoutsò (Mike Francois), ñI use it before training and feel better during my workoutò (Rich Gaspari), and ñI was able to train harder and more oftenò (Charles Clairmonte). (*Id*. at 138-139).

Accordingly, the advertisement teaches the use of Professional Protein for enhancing muscle performance and recovery from fatigue. (Earnest Decl., ¶¶ 27-30). Professional Protein contains the same ornithine alpha-ketoglutarate and ketoisocaproic acid (KIC) ingredients as Mass Fuel, thus invalidating claims 1, 2, 5, 8, 9, and 18 using the same analysis as discussed *supra*. (Earnest Decl., ¶¶ 26-32). The advertisement also invalidates claim 7. (*Id*. at ¶ 31). Claim 7 is a dependent claim of claim 1 with the limitation that the composition contains arginine, one of the ingredients in Professional Protein. (Exh. P, col. 17, ll. 13-14).

3. The January 1995 Flex Magazine Advertisements for National Health Products "Hot Stuff Double X" Anticipate Claims 1, 7, 8, 9 and 18 and Render Claim 10 and 12 Invalid as Obvious.

The ñHot Stuff Double Xò supplement includes over 20 ingredients, including the ingredients:

- OKG
- Arginine Pyroglutamate
- Creatine

(Exh. S at 213-214).

The advertisement states that use of the supplement for 30 days results in:

- 8 to 14% increase in strength levels
- 3 to 5 pounds increase in muscle mass

- ñdramatic increase in recuperation powerò
- Up to three hours of sustained workout energy.

(*Id*. at 177, 214).

Accordingly, the Hot Stuff Double X advertisements teach the use of an amino-acid (cationic or dibasic) / ketoacid combination for enhancing muscle performance and recovery from fatigue, thus anticipating claim 1. (Earnest Decl., ¶¶ 33-38). Arginine is present, thus anticipating claim 7. (*Id*. at ¶¶ 33, 38). OKG is a conjugated compound, thus anticipating claim 8. (*Id.* at ¶¶ 33, 38). The substance is administered orally, thus anticipating claim 9. (*Id*. at ¶¶ 37-38). The substance is to be used on a human subject, thus anticipating claim 18. (*Id.* at ¶¶ 37-38).

4. The February 1994 Advertisement in Flex Magazine for TwinLab Anti-Catabolic Fuel Anticipates Claims 1, 2, 5, 8, 9, 12, and 18 and Renders Claim 10 Invalid As Obvious; The November 1993 Advertisement in Flex Magazine for Weider Performance OKG Anticipates Claims 1, 8, 9, 12 and 18 and Renders Claim 10 Invalid As Obvious.

These supplements differ from those discussed above mainly in that they were amino acid / ketoacid compositions which were provided in capsule form. Accordingly, they directly meet the additional limitation presented in claim 12 of the õ287 patent. Additionally, as these substances are free from the protein content of the powders discussed above, it is readily apparent that one of ordinary skill in the art could prepare a low calorie composition from their contents. (Earnest Decl., at ¶¶ 43, 58). Indeed, a user could easily open the capsule to dissolve the contents in water and consume the composition as a low calorie beverage.

In other respects the anticipation analysis parallels that discussed thus far. The February 1994 advertisement for TwinLab Anti-Catabolic fuel describes this and other supplements in the advertisement collectively as ñPerformance Enhancer Capsulesò

which provide more power, more strength and more endurance and ñenhance performance from the inside out.ò (Exh. T at ñback coverò). The November 1993 advertisement for Weider Performance OKG also presents the supplement in a product line that claims to provide the ability to complete one more set or repetition (e.g., of a weightlifting exercise) and specifically with respect to Performance OKG that a user is ñcranking it outò with the supplement. (Exh. U at 84-85). TwinLab Anti-Catabolic Fuel is described as containing L-ornithine alpha-ketoglutarate, L-glutamine, and ketoisocaproate. (Exh. T at ñback coverò). Accordingly, the advertisement anticipates claims 1, 2, 5, 8, 9, 12 and 18. (Earnest Decl., ¶¶ 39-43). Weider Performance OKG is presumed to contain no other active ingredients and thus anticipates claims 1, 8, 9, 12 and 18. (Earnest Decl., ¶¶ 44-49).

5. The Di Pasquale Reference Anticipates Claims 1, 2, 5, 7, 8, 9, 10, and 18 and Renders Claim 12 Invalid as Obvious.

The book ñThe Anabolic Dietò by Dr. Mauro Di Pasquale was published in 1995 and disclosed a diet regimen for ñthe natural athlete who wants to be the best that he can be naturallyò by optimizing the human bodyøs muscle building mechanism. (Exh. V at 3-7). Dr. Di Pasquale recommends that users take several ñformulasò before, during, or after workouts ñto increase muscle mass and strength by increasing protein synthesis and decreasing protein catabolism.ò (*Id.* at 56-57).

Dr. Di Pasqualeøs ñFormula 1ò is titled ñthe Anticatabolic-Anabolic Compoundò and is comprised of OKG (ornithine alpha-ketogluterate), KIC (ketoisocaproate), glutamine and leucine. (*Id*. at 57). The formula is to be taken just prior to training and to be sipped in water continuously during a workout. (*Id*. at 57). Glutamine is described as essential for building muscle and decreasing muscle breakdown, sparing muscle tissue

and other amino acids that might otherwise be used for glutamine production. (*Id*. at 57-58). The other ingredients are described as stimulating protein synthesis and inhibiting muscle breakdown. (*Id*. at 57).

ñFormula 3ò is labeled ñThe ôInsulin Anabolizerô Compound.ò (*Id*. at 58). It consists of KIC, OKG, arginine, glutamine, and other ingredients. (*Id*. at 58). The stated goal of the formula is ñto increase and maximize the anabolic, muscle building effects of insulin and growth hormone after the workout and during rest.ò (*Id*. at 58). Users are instructed to take the formula immediately after a workout and before bedtime. (*Id*. at 59). Dr. Di Pasquale again notes that glutamine leads to decreased muscle breakdown and increased levels of muscle protein, while arginine helps ñstimulate and maximize the anabolic effects of both insulin and growth hormone.ò (*Id*. at 58).

The use of the formulas as discussed by Dr. Di Pasquale clearly anticipates all of the currently asserted claims of the ô287 patent with the exception of claim 12 (which requires the composition be taken in capsule form). (Earnest Decl., ¶¶ 50-56). The supplements are directed to be used for the purpose of increasing muscle performance or recovery from fatigue. Both supplements contain an amino acid and ketoacid with the amino acid capable of being cationic or dibasic and the two acids in conjugated form (OKG), ketoisocaproic acid (KIC), glutamine, are to be taken orally, and are to be used on a human. Arginine, required by claim 7, is found in Formula 3.

As to claim 12, the preparation of compounds such as the Di Pasquale formulas in capsule form was well known to those of ordinary skill in the art and an obvious variation to use for the consumption of such compounds. (Earnest Decl., ¶ 57). Accordingly, claim 12 of the ô287 patent is invalid as obvious.

6. Claims 10 and 12 of the '287 Patent Are Invalid As Obvious Because the Administration of Ornithine Alpha-Ketoglutarate (or Any Other Compound Disclosed in the Above References and Claimed in the '287 Patent) In a Low-Calorie Beverage or In Capsule Form Was Well Known as of November 13, 1996.

To the extent claims 10 and 12 are not anticipated by the aforementioned publications, they are invalid as obvious. It has long been a trivial matter for one of ordinary skill in the art to prepare a nutritional supplement in a low calorie liquid such as water or to formulate nutritional supplements as capsules. (Earnest Decl., ¶ 58). Several of the aforementioned references disclose the use of supplements as capsules (e.g., TwinLab Anti-Catabolic Fuel, Exh. T) and the preparation of the supplement in water (e.g., Dr. Di Pasquale's formulas or TwinLab Mass Fuel, Exh. V and Q). Though inconceivable that one of ordinary skill in the art would need to combine these references to reach the respective limitations of claims 10 and 12 (i.e., not possess such knowledge him or herself), such a combination would be obvious to anyone seeking to deliver the claimed supplement in low-calorie or easy-to-swallow form. (Earnest Decl., ¶¶ 57-58).

7. The Asserted Claims of the '287 Patent Are Invalid As Obvious Because The Prior Art Publications Suggest the Use of the Claimed Compounds for The Claimed Purposes.

The anticipation of the '287 patent is readily apparent from even a cursory review of the aforementioned publications. However to the extent that any of the claims at issue are not found to be anticipated, the invention of the '287 patent would have been obvious to those of ordinary skill in the art in light of the publications. The references presented clearly disclose the use of the ingredients identified and described in the '287 patent for the benefit of bodybuilders and athletes, thus making formulations attractive to formulators of nutritional supplements in this area. (Earnest Decl., ¶ 59).

Conclusion

For the foregoing reasons, BSN respectfully requests that the Court enter summary judgment that claim 1 of the ô199 is invalid as obvious under 35 U.S.C. § 103 and that the asserted claims of the ô287 patent are invalid as anticipated under 35 U.S.C. § 102(b) or, in the alternative, obvious under 35 U.S.C. § 103.

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Respectfully submitted,

/s/ J. Thad Heartfield

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CERTIFICATE OF SERVICE

The undersigned certifies that all counsel of record who have consented to electronic service are being served with a copy of this document via the Courtôs CM/ECF system per Local Rule CV-5(a)(3) on this the 10th day of July, 2008. Any other counsel of record will be served by first class mail.

/s/ J. Thad Heartfield
J. Thad Heartfield